VOL. VIII, No. 2 FEBRUARY, 1947

BORDEN'S REVIEW *of* NUTRITION RESEARCH

VITAMIN REVIEW, I.

BORDEN'S REVIEW
of
NUTRITION RESEARCH

Reviews and summaries of research information concerning nutrition and foods. Published monthly, except July and August, by THE BORDEN COMPANY; officers of the Company: Theodore G. Montague, president; E. L. Noetzel, treasurer; T. D. Waibel, secretary. Editorial office: 350 Madison Avenue, New York 17, N. Y.

VITAMIN REVIEW, I.

By **RUTH WOODS**

In the history of nutrition, the year 1913 stands out as a significant date. In that year, Casimir Funk coined the word "vitamine." The term "vitamine" crystallized a rapidly growing, but still nebulous concept among nutritional chemists that minute traces of certain unidentified natural constituents of food exerts a profound influence on body metabolism and that the absence of these mysterious elements in the diet constitutes a major threat to life. From that time until the 1930's, vitamin research progressed steadily, but slowly, largely because of lack of information concerning the exact nature of these unknown dietary elements.

Beginning with 1930, however, came the development of vitamin concentrates, the isolation of individual vitamins in purified form and, finally, the resolution of the chemical identity of these compounds. The knowledge that the vitamins are specific chemical compounds, some of which were long before known to chemists (as for example, nicotinic acid) made their synthesis possible.

The modern era in vitamin research began with the availability of pure vitamins—either as the naturally isolated substance or the synthetic product. From then on, knowledge of the chemistry and physiology of the vitamins grew at a phenomenal rate. More vitamin discoveries have been made in the past decade, particularly in the past few years, than during all the other years of vitamin research.

The material presented in these pages constitutes the first half of a two-part review designed to serve as a concise and ready reference guide to the vast amount of data which have accumulated on the subject of the vitamins from 1913 until the present. It is not the aim of the Vitamin Review to be all-inclusive in scope, but rather to summarize significant and pertinent information concerning the more well-established members of the vitamin family.* This section of the Vitamin Review will include thiamine, riboflavin, nicotinic acid, pantothenic acid, pyridoxine, *p*-aminobenzoic acid, inositol, biotin and choline. The folic acid group, the other water soluble vitamins and the fat soluble vitamins will be described along with the other vitamins, in the second part of the Review.

---

*A list of the newer unidentified or "postulated" vitamin or vitamin-like factors will be included at the end of the Review for the sake of completeness and as an indication of possible future pathways of vitamin research.

Thiamine:

Thiamine chloride or vitamin B_1 (also known as aneurin in the British literature) is commonly called the antineuritic or anti-beriberi vitamin. Its chemical formula is known, it has been isolated in pure form and has also been synthesized. Thiamine is a pyrimidine-thiazole compound, available commercially as the salt, thiamine, hydrochloride. It is represented structurally as shown in Fig. 1.

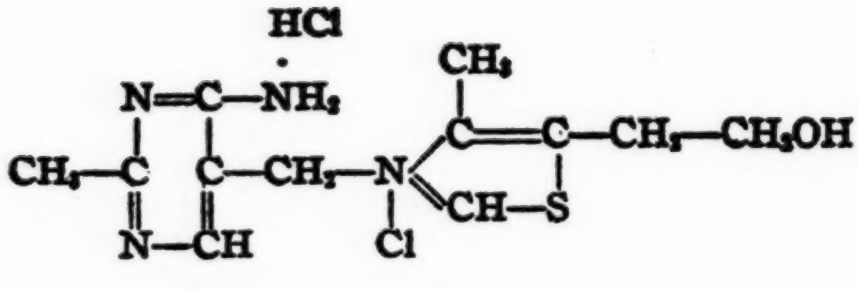


FIG. 1 THIAMINE HYDROCHLORIDE
4-Methyl-5-β-hydroxy-ethyl-N-{[2-methyl-4-amino-pyrimidyl-(5)]-methyl}-thiazolium-chloride-hydrochloride

Thiamine is soluble in water and relatively stable in dry heat, but it is readily destroyed in foods during cooking and canning processes. Destruction is retarded in acid media and appreciably hastened by the presence of alkalis.

Thiamine is a dietary essential for man, for birds and for all other non-ruminant animals, as well as for many plants and microorganisms. Sheep and cattle obtain sufficient amounts of the vitamin by bacterial synthesis in the rumen, and therefore do not require its presence in the diet.

Functions: Thiamine is concerned specifically with the intermediate metabolism of carbohydrate in all living cells, chiefly as part of the enzyme system *(cocarboxylase)* involved in the oxidation of pyruvic acid. It is, therefore, essential for the normal functioning of all body organs and tissues. Vitamin B_1 deficiency in man affects first of all the emotions and the nervous system. Mild deficiency produces the mental symptoms of neurasthenia as well as loss of appetite, general weakness, fatigue and lassitude, gastrointestinal disturbances (nausea, constipation), muscular weakness, pains and numbness in the arms and legs, disturbances in heart function and in circulation, palpitations, loss of weight, edema and shortness of breath. Severe thiamine deficiency causes beriberi which is characterized by polyneuritis, neuralgia, edema, muscular incoordination and heart failure resulting from abnormal enlargement of the heart. Corresponding symptoms referable to the nervous system are observed in other animal species. Thiamine acts as a growth-stimulant for plant roots as well as for certain microorganisms.

Requirements: Thiamine is not stored to any great extent in the body, excesses usually being destroyed or excreted. The supply must, therefore be

replenished from day to day. The amount needed varies with a number of factors, such as the total amount of food ingested, particularly carbohydrate, and the level of metabolism. The metabolic rate, in turn, is influenced by such factors as physical activity, fever, pregnancy, thyroid function and alcoholism. Heightened metabolism or high carbohydrate intake or interference with normal utilization because of disease increase the need for thiamine. The minimum adult requirement* for thiamine is 1.0 mg. per day; the recommended daily allowance† ranges from 1.1 to 2.0 mg. depending upon age, sex and activity. No toxic reactions from massive, therapeutic doses have been reported in man; experimentally, however, massive doses of thiamine resulted in toxic reactions in rats.

Sources: Important food sources of thiamine (either because of richness of thiamine content or because of widespread use in the average diet) include dried yeast, whole wheat bread, wheat and cereal germ, enriched bread, lean meat (particularly liver), nuts and legumes, powdered whey, milk, eggs and potatoes. Synthetic thiamine is also available in graded dosages for supplementary and therapeutic purposes.

Antagonists: Some kinds of raw fish contain an enzyme which destroys thiamine and which therefore produces the effect of a thiamine deficiency. Also, certain structural analogs of thiamine, such as the compound, pyrithiamine, interfere with the body utilization of the vitamin by substituting for thiamine in enzyme systems which require the vitamin as an integral component. Pyrithiamine is similar enough in structure to thiamine to replace it chemically in the enzyme-complex. But since pyrithiamine has no vitamin activity, its presence in the enzyme complex is useless. This renders the enzyme just as ineffective as would an absolute deficiency of thiamine.‡

---

*U. S. Food & Drug Administration.
†National Research Council, Food & Nutrition Board.
‡*cf. Borden's Review of Nutrition Research,* October 1946, "The Anti-Vitamins."

Riboflavin:

Riboflavin or vitamin B_2 is the major constituent of the so-called "vitamin B_2 complex." This fraction includes most of the B vitamins other than thiamine and is distinguished from thiamine by its relative stability to heat. Riboflavin has been isolated and synthesized. It is an alloxazine compound, one of a large group of flavin pigments, and is represented by the structural formula shown in Fig. 2.

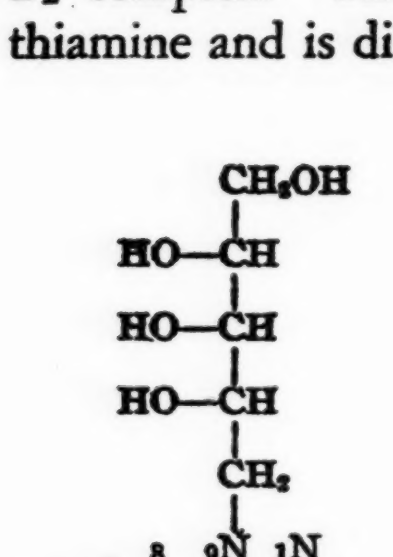


FIG. 2 RIBOFLAVIN
6, 7-dimethyl-9-d-ribityl-iso-alloxazine

Riboflavin is relatively heat-stable, slightly soluble in water and, in solution, is readily destroyed by exposure to light, especially in the presence of alkali. In foods such as meat, it is not readily destroyed by home stewing methods, but there are appreciable losses when meats are roasted or fried. About 5 to 20 per cent losses of riboflavin occur in canning processes.

Riboflavin is a dietary essential for man as well as for most other animal species—pig, dog, chick, turkey, rat. It is also essential for some, but not all, species of microorganisms. Sheep and cattle obtain their requirements by bacterial synthesis in the intestine.

Functions: Riboflavin, as well as related flavoprotein derivatives, functions as a hydrogen transporter in the body. It is capable of undergoing oxidation and reduction reactions (donating and accepting hydrogen) and thereby plays a significant role in biological respirations. The vitamin activity of riboflavin is apparently related to the function of the "yellow respiratory enzyme" of which it is an integral part. The yellow enzyme is normally present in all tissue cells and acts in conjunction with other cellular catalysts (dehydrogenase and a coenzyme) in the complex reactions involved in cellular oxidation. Specifically the yellow enzyme is alternately oxidized and reduced, its function thereby being somewhat similar to that of hemoglobin. It is believed that this enzyme is essential for the carrying on of oxidation processes in tissues which are poorly supplied with blood, such as the cornea of the eye. This would seem to be confirmed by the fact that one of the characteristic, early symptoms of riboflavin deficiency is the development of corneal vascularization (bloodshot eyes)—a symptom which disappears promptly upon administration of dietary riboflavin. It has been suggested that the invasion of the cornea by blood vessels may be an attempt on the part of the body to supply oxygen-containing hemoglobin

to these normally bloodless tissues in order to compensate for the lack of oxygen caused by the absence of the yellow enzyme.

The general effects of severe riboflavin deficiency in all species requiring it are cessation of growth in the young and sudden death in the adult. Rats develop involution of the thymus gland and atrophy of the testis, as well as baldness, cataract of the eye and vascularization of the cornea. Fowl require riboflavin for proper egg production and hatchability, as well as for the prevention of a specific nerve paralysis. Riboflavin deficient turkeys develop a characteristic dermatitis.

In man, riboflavin deficiency causes cheilosis, a condition of the mouth, tongue and lips characterized by abnormal redness and cracks in the corners of the mouth as well as fissures and scaly desquamations around the folds of the nose and ears. Eye disturbances include itching, burning, a sensation of roughness of the eyes, sensitivity to light, and vascularization and opacity of the cornea.

Requirements: Riboflavin requirements, like those of thiamine, are in general related to body size and weight, to the amount of food ingested and to the general metabolic level of the body. Minimum daily requirements for adolescents and adults are 2.0 mg. per day; the recommended allowance from about 1.5 to 2.5 mg. per day depending on age, sex and activity, increasing to 3.0 mg. during pregnancy and lactation. No toxic reactions have been observed with fairly massive doses.

Sources: Riboflavin is widespread in nature, occurring in most plants and animals. Growing fermentation bacteria are the richest known source. Good food sources are liver, kidney and heart meats, milk, powdered whey, cheese, eggs, fish, oysters, yeast, dried prunes, enriched white bread, whole grains and germ, peanuts, peas, lima beans, bananas and ice cream. Synthetic riboflavin in crystalline form is commercially available for special purpose use.

Antagonists: At least three, and probably more, compounds structurally related to riboflavin have been found to inhabit its action and to precipitate symptoms of riboflavin deficiency. These are *iso*-riboflavin, the dihydrophenazine analogue of riboflavin (also other phenazine derivatives), and the dichloro analogue of riboflavin. The principle involved is the same as that described for the thiamine inhibitors.

Nicotinamide:

Nicotinic acid, popularly known as niacin, is the chief factor involved in the prevention and cure of pellagra, although it is now known that certain aspects of the disease respond specifically to thiamine or riboflavin therapy and are unaffected by nicotinic acid. It is a pyridine compound and has been isolated and synthesized. Nicotinic acid is available commercially as the amide in which form it may be administered without the undesirable skin flushing effects which accompany the administration of large amounts of the acid. Nicotinic acid amide is known popularly as niacinamide or nicotinamide. The formulas for the acid and amide are:

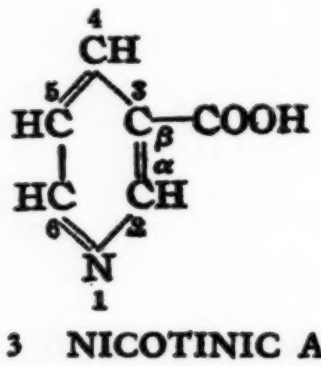
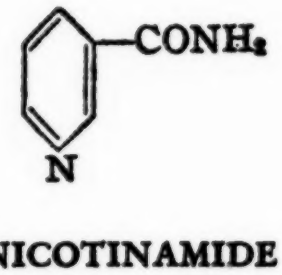


FIG. 3 NICOTINIC ACID
pyridine-3-carboxylic acid



NICOTINAMIDE
pyridine-3-carboxylic acid amide

Functions: Like thiamine and riboflavin, the importance of nicotinic acid lies in its relation to certain vital enzyme systems. Specifically, it is the functional group of coenzymes I and II (diphosphopyridine nucleotide, DPN, and triphosphopyridine nucleotide, TPN, respectively). These substances play an important part in carbohydrate metabolism and tissue respiration and probably act in a manner similar to that of riboflavin. That is, they act as hydrogen carriers.

Niacin deficiency in dogs produces the disease known as blacktongue. In man, niacin deficiency precipitates the classic "three D's" of pellagra: dementia, diarrhea and dermatitis. The polyneuritis and neurasthenia of thiamine deficiency as well as the cheilosis of riboflavin deficiency are almost always also superimposed upon the pellagra picture. The dementia of pellagra begins with confusion, dizziness, poor memory and depression. It progresses to violent psychotic states characterized by hallucinations and delusions of persecution. The alimentary tract symptoms culminating in diarrhea are preceded by soreness, burning or inflammation of the mouth, tongue, gums, pharynx, stomach and intestines. Vincent's angina is a frequent complication. The dermatitis is a characteristic, symmetrical rash which appears simultaneously on both sides of the body, on the backs of the hands, forearms, elbows, knees. The skin is rough, cracked, scaly and red. The areas of lesions are very sharply demarcated from the surrounding normal

skin. Sunlight aggravates the lesions. Niacin has also been reported to be of value in treating x-ray sickness. Because of its pharmacological vasodilator action, the acid *(not amide)* has been used in treating Meniere's disease.

Requirements: All living organisms require nicotinic acid. Dogs, pigs, monkeys and man require it in the diet whereas rats and other species apparently synthesize the vitamin internally. The recommended daily allowance for nicotinic acid for adults ranges from 11 to 20 mg. depending upon age, sex and activity. (N.B. One hundred grams of nicotinamide are equivalent to 100.8 grams of nicotinic acid). An intake of about 1,000 times the amount of nicotinic acid which is normally consumed in foods is considered relatively nontoxic. Higher doses are toxic. Dogs kept on 2 grams of nicotinic acid per day die within 20 days. In humans, large oral doses of nicotinic acid cause flushing, burning, itching and sensations of local heat in the skin. Since nicotinamide does not produce these symptoms, it is preferred for clinical use.

Sources: Good food sources are beef and hog liver, yeast, kidney, lean meats, chicken, peanuts, whole meat, salmon, eggs, milk, coffee, green vegetables. Niacin and niacin amide are both available as the synthetic crystalline compounds.

Antagonists: Nicotinic acid is inhibited by the structurally related compounds, 3-acetylpyridine and 3-pyridine sulfonic acid.

Recent studies with rats and other animals have shown that niacin requirements are influenced in rather complex ways by dietary corn or maize or by the amino acid tryptophane. Corn tends to increase niacin requirements. On the other hand tryptophane appears to function as a precursor of niacin and also to reverse the inhibitory effects of corn. A number of possible explanations for the effect of corn in increasing niacin requirements have been offered: (1) The presence in corn of a niacin inhibitor; (2) a depression by corn of the bacterial synthesis of niacin in the intestine; (3) the low tryptophane content of corn; (4) and a general amino acid imbalance in corn proteins.

Pantothenic Acid:

Pantothenic acid, also known as the "filtrate factor" and the "chick antidermatitis factor" is a constituent of the original yeast growth factor "bios." It is an organic acid, soluble in water and, in solution, unstable to heat. It is available commercially as the calcium salt, calcium pantothenate. Pantothenic acid has been synthesized. Fig. 4 shows the formula.

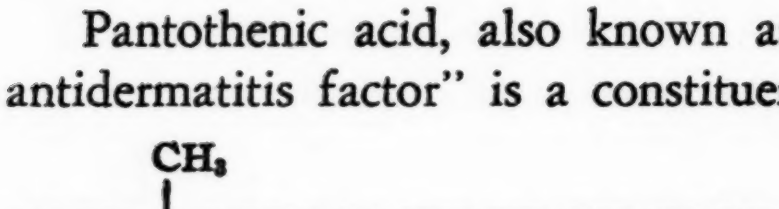


FIG. 4 PANTOTHENIC ACID
2-4-dihydroxy-3-3-dimethylbutyryl-beta-alanine

Functions: The biochemical role of pantothenic acid is still obscure. It is known to be essential for all living organisms, including man, but the scope of its activity has not been clearly defined except for a few species. Chicks require pantothenic acid to prevent a typical dermatitis around the eyes, mouth and toes. Pantothenic acid deficient chicks also develop certain degenerating changes in the spinal cord, fatty livers and involution of the thymus. Pantothenic acid also seems to be essential for reproduction and for proper hatchability of eggs. Rats, mice and silver foxes deficient in pantothenic acid develop gray hair ("nutritional achromotrichia"). Claims made for the anti-gray hair value of pantothenic acid for humans have been largely unsubstantiated. The vitamin also prevents "spectacled eye condition" in rats as well as severe hemorrhagic and degenerative changes of the adrenal glands. The role of pantothenic acid in human nutrition is not known. Its probable significance is indicated by the fact that blood levels of pantothenic acid are lowered in pellagra, beriberi and ariboflavinosis. A possible function may be to promote intestinal synthesis of other B vitamins by providing proper nutrition for the intestinal flora. It is also thought to be involved in the utilization of other vitamins, particularly riboflavin.

Requirements: Requirements for pantothenic acid have not been established except for the chick and the rat. About 500 micrograms per 100 grams of feed appear to be necessary to prevent dermatitis and about 600 micrograms to insure optimal growth. It is non-toxic in large doses.

Sources: Pantothenic acid is extremely widespread in occurence as its name ("from everywhere") implies. Best sources include egg yolk, liver, kidney, dried whey, yeast, milk, buttermilk, molasses, salmon, rice bran, lean meat, oatmeal, broccoli, cabbage, cauliflower, potatoes, tomatoes, corn, cucumbers, peas. Crystalline calcium pantothenate is available commercially.

Antagonists: Pantothenic acid is inhibited by thiopanic acid and by phenylpantothenone.

Para-Aminobenzoic Acid:

Para-aminobenzoic acid (PABA) has been known to organic chemists since its synthesis in 1863, but it was not until 1941 that its status as a vitamin was postulated. In 1940 it was discovered that PABA reversed the action of sulfanilamide. It was suggested the PABA is an essential metabolite for bacteria and that the bacteriostatic action of the sulfonamides was due to a competitive struggle between the two structurally similar compounds for a place on an essential enzyme (the beginnings of the anti-vitamin theory). In the following year PABA was shown to play a part in rat and chick nutrition and its role as a vitamin has been energetically debated ever since. Para-aminobenzoic acid is water-soluble and is available in crystalline form. Its formula is shown in Fig. 5.

FIG. 5 PARA-AMINOBENZOIC ACID

Functions: The biochemical role of para-aminobenzoic acid is extremely obscure. It is thought to be involved, like the other B vitamins, in an enzyme system (possibly phenolase?), particularly in view of the evidence of its behavior with the sulfonamides. It has been implicated in pigment metabolism and is thought to have some influence on melanin* deposition, thereby possibly being involved in the phenomena of sunburn and graying of hair. Although PABA has been shown to be an anti-gray-hair factor for the rat, claims for a similar role in man have not been substantiated. Like pantothenic acid, it is thought to be significant through its effect on the intestinal bacteria which require it in order to permit them to synthesize other essential vitamins. PABA is required also for proper growth of the chick and for certain micro-organisms. A PABA derivative, the peptide para-aminobenzoyl-*l*-glutamic acid has been reported to have almost 10 times the anti-sulfonamide activity of the original amine. It is interesting to note that PABA is closely related to the recently synthesized vitamin, pterolyglutamic acid (folic acid). Recent studies have demonstrated a clinical role in man in combatting rickettsial infections such as Rocky Mountain spotted fever.

Requirements: Requirements of PABA are not known. In rats, 0.75 mg. per day cures nutritional achromotrichia (gray hair). Chicks usually receive about 30 mg. per 100 grams of ration. PABA is relatively non-toxic.

Sources: Yeast, rice bran and polishing, whole wheat and germ, molasses, are other good sources of B complex vitamins.

Antagonists: Sulfonamides.

---

*The substance responsible for color of skin, hair and eyes.

Biotin:

Biotin, popularly known as the anti-egg white injury factor, also as vitamin H and coenzyme R, was synthesized recently. It is another one of the constituents of the original "bios" concentrate and possesses such remarkable potency that one part in four hundred billions will stimulate the growth of certain yeasts. Its formula is shown in Fig. 6.

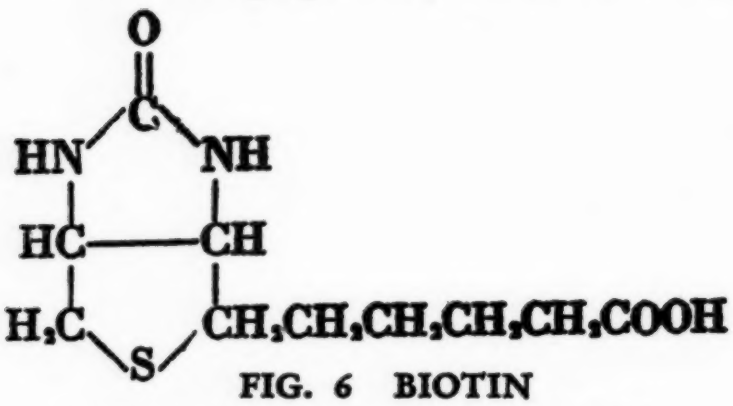


FIG. 6 BIOTIN

Hexahydro-2-oxo-1-thieno (3, 4)-imidazole-4-valeric acid

Functions: The biochemical role of biotin has not yet been clearly defined. The vitamin is believed to be involved in the mechanisms of fat metabolism. The feeding of biotin to rats has been found to result in an abnormal increase in the fat and cholesterol synthesis in the liver. This type of fatty liver can be controlled by administering the lipotropic secretion of pancreas—lipocaic. Biotin deficiency in chicks and rats is manifested by a characteristic seborrheic skin disease quite unlike the dermatitis of pellagra or acrodynia. In addition, rats develop a typical denudation around the eyes—"spectacle eye" condition. Experimental biotin deficiency in man resulted in skin changes, extreme lassitude, muscle pains, stomach ache, and loss of appetite. All of these symptoms disappeared rapidly upon parenteral administration of biotin. Clinically biotin has been used with some degree of success in acne, seborrheic baldness and psoriasis.

Requirements: Biotin is required by all animal species investigated and by certain microorganisms. Cattle synthesize the vitamin in the rumen. Man responds favorably to doses of 150-300 micrograms per day; chicks need about 2.5 to 10 micrograms and rats about 1-3 micrograms per day.

Sources: Liver, kidney, eggs, vegetables, grains, nuts, milk, yeast. Synthetic biotin and biotin concentrates are available commercially.

Antagonists: A number of inhibitors modelled on the biotin molecule have been prepared experimentally. These include, among others, desthiobiotin and biotin sulfone. Aside from its inhibition by structural analogues, biotin is chemically inactivated by forming a stable complex with avidin, a protein compound occurring in raw egg white. The administration of large amounts of avidin to experimental animals and to man on biotin low diets produces symptoms of biotin deficiency. The discovery of the biotin-avidin complex is the first historical example of the existence of an antivitamin.

Choline:

Choline, a well-known constituent of lecithin, is another comparative newcomer to the vitamin B family, although its vitamin nature has sometimes been questioned on the grounds that the amounts required are excessively large according to the accepted definition of a vitamin. Its formula is shown in Fig. 7.

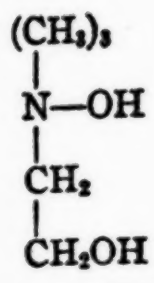


FIG. 7 CHOLINE
Hydroxyethyl-trimethyl-ammonium hydroxide

Functions: The primary role of choline is that of a biological methylating agent. It is replaceable in this activity to varying extents by the amino acid, methionine and by betaine and certain other methylated compounds. In the dietary absence of methionine, the essential amino acid, choline donates methyl groups to the non-essential homocysteine. This enables the body to convert homocysteine to methionine, and helps maintain animals which would otherwise fail to grow. In addition choline is capable of preventing and curing fatty livers and certain types of liver cirrhosis. It is also a vital factor in preventing a characteristic hemorrhagic kidney disease in young rats. Choline is also important in poultry nutrition as an anti-perosis factor and as an essential to proper egg production. Not all of its behavior can be explained on the basis of its methyl donating capacity, however, since certain non-methyl containing analogues of choline can substitute for choline as lipotropic, anti-hemorrhagic and anti-perosis agents. Being devoid of labile methyl groups, however, these compounds cannot replace choline as a growth essential in a choline and methionine free diets containing homocysteine. Physiologically, choline serves as a building unit in many phosphatides and is present in the phospholipids of almost all cells. It regulates the turnover of fat and phospholipid in the liver (lipotropic activity). Choline is utilized after acetylation as a blood-pressure reducing substance. Further, acetylcholine is intimately involved in the propagation of nerve impulses.

Requirements: Choline is required by all animals and by certain bacteria. The young of the species requires more choline than does the adult organism. Rats require about 10-20 mg. per day; dogs, about 35 mg. per kilo of body weight; chicks need about 75 mg. daily. The human requirement is not known. Methionine or betaine can be substituted for choline, but are only about 30 per cent as efficient.

Sources: Liver, heart, kidney, sweetbreads, brain, egg yolk, tongue, yeast, fish, fruits, grains, meat, milk, nuts, roots and green, leafy vegetables. Choline is available commercially.

Pyridoxine:

Pyridoxine, the eluate factor, is also known as vitamin B_6 or adermin (because it prevents a typical skin disease in rats). It is water-soluble and heat-stable, but is readily destroyed by light. It has been synthesized and is usually supplied as the hydrochloride. Following are the formulas for pyridoxine and two physiologically important related compounds, pyridoxal and pyridoxamine.

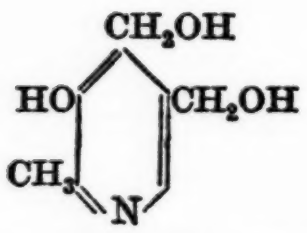
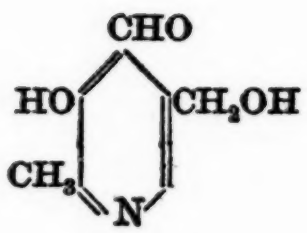
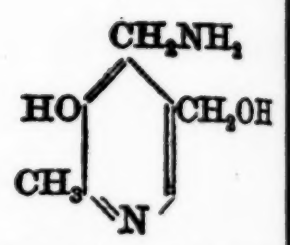


FIG. 8 PYRIDOXINE
2-methyl-3-hydroxy-4-5-dihydroxy methyl-pyridine



PYRIDOXAL



PYRIDOXAMINE

Functions: Pyridoxine is thought to be involved in the utilization of the unsaturated fatty acids and in certain essential transamination reactions in protein metabolism. Two recent suggestions link the vitamin with (1) a coenzyme involved in the decarboxylation of tyrosine and (2) a transamination coenzyme. In both instances pyridoxine itself appears to be inactive, the biologically active agent being the closely related compound, pyridoxal (see Fig. 8). Pyridoxal appears to function in the tyrosine cycle, while the transamination activities seem to depend on the interconversion of pyridoxal and pyridoxamine. A highly active form of pyridoxine (with respect to microbial growth) known as "pseudopyridoxin" was recently identified as a mixture of pyridoxal and pyridoxamine. It is generally believed that pyridoxal is the active form of vitamin B_6, pyridoxal phosphate being a coenzyme of at least three amino acid decarboxylases.

Pyridoxine prevents a typical skin disease in rats (acrodynia), a characteristic anemia in dogs, and pathological changes in heart muscle and spinal cord of rats. Rats, dogs and pigs deprived of pyridoxine became subject to epileptiform fits which may be brought on by any slight stimulus, such as loud noises. The role of vitamin B_6 in humans has not been established. Scattered clinical reports have hinted at its possible value in treating certain nervous and muscular disorders—Parkinson's disease, myasthenia, epilepsy, muscular dystrophy—and certain types of anemia. It has also been used as an effective adjunct to other B vitamin therapy in pellagra, beriberi and ariboflavinosis. Because of its sedative effect on humans, it has also been used with some success in combating the nausea and vomiting of pregnancy.

Requirements: Chicks require about 30 micrograms per day; rats about 10. No requirement has been established for man, but clinical doses have ranged from 10-100 mg. per day. Pyridoxine is relatively non-toxic. When injected, it must be administered intravenously; intramuscular injections cause severe pain.

Sources: Egg yolk, wheat germ, yeast, liver, kidney, meat, milk, legumes, whole grains.

Inositol:

Inositol, the mouse anti-alopecia (baldness) factor, is the optically inactive form of a hexahydroxy cyclohexane, represented by formula in Fig. 9.

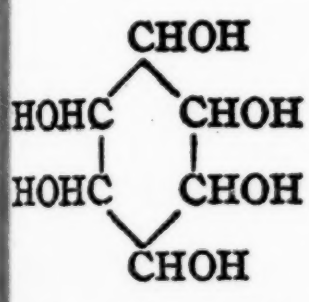


FIG. 9 INOSITOL

It is a highly stable compound and is readily soluble in water. Though known to organic chemists for many years, its vitamin potentialities were only comparatively recently established.

Functions: The chief known role of inositol is as a preventor of loss of hair in mice. It is also believed to be a factor in stimulating gastro-intestinal motility and in regulating certain phases of fat metabolism. Inositol is recognized as a lipotropic factor, although it differs from the other lipotropic factors, choline and methionine, both in its mode of action and in the type of fatty liver which it prevents. Inositol occupies a position midway between the anti-alopecia factors (PABA, pyridoxine and pantothenic acid) and the lipotropic factors, having functions in common with both groups.

Requirements: Requirements for inositol are not known. Deficiency symptoms in mice have been cured by feeding 10 mg. of inositol per 100 grams of food; in rats, by daily dose of 20 mg.

Sources: Yeast, whole grains, milk, meats, nuts, fruits, vegetables. Synthetic inositol is also available commercially.

Although it has not been stated specifically for each vitamin, it is generally recognized that each of the B vitamins is an important factor in animal growth and, frequently, in reproduction and lactation as well. Deficiency symptoms of many of these vitamins include many scattered effects on various enodocrine glands and on the blood and nervous system, although space has not permitted a detailed recording of these isolated but nonetheless significant effects.

Printed in U.S.A.